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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,037	07/13/2006	Jeffrey L. Southard	560252000800	1724

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
12/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,037	SOUTHARD ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *4-8,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 9-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1108,0509*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1–22 are pending.

Election/Restrictions

Applicant's election without traverse of group I, claims 1–16(in part), 17–19 and 20 (in part), and the species intravenously, diuretics and surface active agents in the reply filed on 10/14/2009 is acknowledged.

Claims 4–8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/14/2009.

Claims 21 and 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/14/2009.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1–3 and 9–20 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment, does not reasonably provide enablement for a method of prevention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

HF is a terminal condtion, according to the specification (paragraph [0005]). There are no working examples of prevention. The examiner is aware working examples are not required. Lack of a working example is, however, a factor to be considered. The skilled artisan is left to his own devices and through trial and experimentation is left to determine how to achieve such prevention.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to use the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17–19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "several" in claim 17 is a relative term which renders the claim indefinite. The term "several" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 18 and 19 depend from claim 17, and thus share this defect with claim 17. The metes and bounds are not clearly set forth.

The term "improves the quality of life" in claim 19 is a relative term which renders the claim indefinite. The term "improves the quality of life" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2 and 10–20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stevenson (Int J Cardiol. 1992 Dec;37(3):407-14), Anand (J Am Coll Cardiol. 1991 Jan;17(1):208-17), Shekhar (J Cardiol. 1991 Apr 1;67(8):732-6) and Gennari (Cardiovasc Res. 1990 Mar;24(3):239-41).

Stevenson infused CGRP via a peripheral venous cannula at a rate of 0.6 µg/min (=600 ng/min) to patients with congestive cardiac failure . The intermittent infusion group was infused with CGRP for 8 h at the start of the 2 study days. See page 408, right column. The intermittent regimen was well tolerated, whereas the continuous regimen was poorly tolerated (page 410). The vasodilator properties of CGRP produced a useful improvement in left ventricular function in heart failure patients (page 412, left column).

Anand teaches that CGRP may be useful in some forms of heart failure (Abstract). Anand administered CGRP to patients with congestive HF. All were taking diuretics. See paragraph bridging pages 208-209. The peptide was infused into a forearm vein using an infusion pump. Incremental infusions of CGRP at the dose of 0.8, 3.2 and 16 ng/kg/min were made, the first two doses were infused for 10 min each. The highest dose was infused for 20 min.

Shekhar infused CGRP into a forearm vein of patients with heart failure using an infusion pump at a does of 8.0 ng/kg/min for 8 h (paragraph bridging pages 732-733), or about 500 ng/min, assuming a 70 kg patient. The dose was midway between the low doses (0.8 and 3.2 ng/kg/min) high dose (16 ng/kg/min) used in previous (Anand (1991)) regimens (page 735, left column). Shekhar concludes that in patients with HF, CGRP has sustained beneficial effects; CGRP also increases renal blood flow and glomerular filtration (Abstract). According to Shekhar, all of the patients that received CGRP were taking diuretic drugs (page 732, right column, full paragraph 2).

Gennari gave CGRP (12.5 μg/h) (≅208 ng/min) by IV infusion for 24 h to patients with congestive HF. CGRP improved myocardial contractility in patients with congestive heart failure. See the Abstract. Body weight was 44-66 kg (page 239, right column, full paragraph 1). The patients were given CGRP by IV minipump infusion for 24 h (page 239, right column, full paragraph 2). Congestive HF is usually caused by reduced cardiac output as a result of impaired cardiac contractility (page 239, paragraph bridging left and right columns).

Stevenson, Anand, Shekhar and Gennari do not teach the specific dosages for the specific times recited in claims 1, 16, 17 and 20. However, Stevenson, Anand, Shekhar and Gennari do teach the general conditions of administering CGRP for the treatment of HF. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. The normal desire of artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of conditions is the optimum combination of dosages and lengths of administration of CGRP to HF patients.

As noted above, Anand and Shekhar disclose that the HF patients given CGRP were also taking diuretics. It is further noted that claim 11 encompasses all conceivable orders of performing the administration of CGRP and the at least one drug. The selection of any order of performing the order of administration of the CGRP and the at least one drug is prima facie obvious in the absence of new or unexpected results.

As noted above, Shekhar teaches that CGRP also increases renal blood flow and glomerular filtration, indicating that the limitations of claim 12 would naturally flow from following the teachings of the prior art.

The examiner considers the limitations in claims 13–15 and 18 obvious because an artisan would be motivated to administer CGRP to whomever is afflicted with HF, wherever whomever is so afflicted, and for such a duration that would achieve treatment.

As noted above, the metes and bounds of “improves the quality of life" are not clearly set forth. Stevenson, Anand, Shekhar and Gennari note beneficial effects when CGRP is administered to HF patients. Therefore, the examiner concludes that Stevenson, Anand, Shekhar and Gennari teach that CGRP “improves the quality of life.” Alternatively, Stevenson, Anand, Shekhar and Gennari suggest CGRP for the treatment of HF. Therefore, improving the quality of life would naturally flow from following the teachings and/or suggestions of the prior art.

The invention is prima facie obvious over the prior art.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stevenson (Int J Cardiol. 1992 Dec;37(3):407-14), Anand (J Am Coll Cardiol. 1991 Jan;17(1):208-17), Shekhar (J Cardiol. 1991 Apr 1;67(8):732-6) and Gennari (Cardiovasc Res. 1990 Mar;24(3):239-41) as applied to claim 1 above, and further in view of Heim (U. S. Patent No. 5126134), Young (U. S. Patent No. 4627839), Strom (U. S. Patent No. 5336489) and Torgerson (U. S. Patent No. 5820589).

Stevenson, Anand, Shekhar and Gennari teach the infusion of CGRP to HF patients, as discussed above. Although Anand, Shekhar and Gennari teach administration of CGRP to HF patients by infusion pumps, Stevenson, Anand, Shekhar and Gennari do not expressly teach administration via a constant rate pump, a variable rate pump, a programmable pump, or an osmotic pump. However, administering a drug via a constant rate pump, a variable rate pump, a programmable pump, or an osmotic pump is old, well know, and widely used in the art. See, for example, Heim, column 14,

lines 4-5; Young column 1, lines 10-15; Strom, column 6, lines 41-45; Torgerson, column 1, lines 15-20. Such pumps would provide accurate long term medication without the need for constant nursing supervision. See, for example, Young column 1, lines 10-15. Heim, Young, Strom and Torgerson do not teach the infusion of CGRP to HF patients.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to infuse CGRP to HF patients, as taught by Stevenson, Anand, Shekhar and Gennari, and to modify that teaching with a constant rate pump, a variable rate pump, a programmable pump, or an osmotic pump, as taught by Heim, Young, Strom and Torgerson, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because such pumps would provide accurate long term medication without the need for constant nursing supervision. The invention is prima facie obvious over the prior art.

Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stevenson (Int J Cardiol. 1992 Dec;37(3):407-14), Anand (J Am Coll Cardiol. 1991 Jan;17(1):208-17), Shekhar (J Cardiol. 1991 Apr 1;67(8):732-6) and Gennari (Cardiovasc Res. 1990 Mar;24(3):239-41) as applied to claim 1 above, and further in view of Chen (U. S. Patent No. 6525102).

Stevenson, Anand, Shekhar and Gennari teach the infusion of CGRP to HF patients, as discussed above. Stevenson, Anand, Shekhar and Gennari do not expressly teach combining CGRP with surface active agents.

The addition of surfactants (i.e., surface active agents) to pharmaceutical compositions comprising polypeptides is well known in the art. See, for example, Chen, which teaches the use of surfactant for stabilizing and/or protecting the polypeptide (column 2, penultimate paragraph; column 10, full paragraph 1; paragraph bridging columns 10-11). Chen does not teach the infusion of CGRP to HF patients.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to infuse CGRP to HF patients, as taught by Stevenson, Anand, Shekhar and Gennari, and to modify that teaching by combining the CGRP with a surfactant, as taught by Chen, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to stabilize and/or protect the CGRP. The invention is prima facie obvious over the prior art.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY NICKOL, CAN BE REACHED AT (571)272-0939.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-0835.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

/DAVID S ROMEO/
PRIMARY EXAMINER, ART UNIT 1647

DSR
DECEMBER 18, 2009